Marketing authority for racemate does not invalidate SPC for its enantiomer

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Generics (UK) Ltd v Daiichi Pharmaceutical Co Ltd (1) and Daiichi Sankyo Co Ltd (2) [2009] EWCA Civ 646

Court of Appeal (Jacob, Ward & Lloyd LJJ)

Judgment date 2 July 2009

Daiichi owned a patent concerning levofloxacin, an enantiomer of the racemic mixture, ofloxacin. Daiichi also owned a Supplementary Protection Certificate (SPC), based on the patent and the marketing authorisation it had obtained for levofloxacin. Generics UK claimed that the patent was obvious over ofloxacin and that the SPC was wrongly granted because it was not based on the first marketing authorisation for the product, which Generics claimed was the earlier marketing authorisation that had been obtained for the racemate (which contains levofloxacin). The judge found both the patent and SPC valid.

Background

The defendants (Daiichi Pharmaceutical Co Ltd and Daiichi Sankyo Co Ltd) owned a patent which disclosed levofloxacin, the S(-) enantiomer of the racemic ofloxacin. Levofloxacin had proved to be a superior anti-microbial to ofloxacin or the R(+) enantiomer. A marketing authorisation was granted for levofloxacin and the defendants obtained an SPC based on this and the patent. The patent had expired but the SPC was still in force.

According to the SPC Regulation (EEC/1768/92), an SPC shall be granted if:

- a. the active ingredient or a combination of active ingredients (the "Product") is protected by a patent in force,
- b. there is a valid marketing authorisation for that Product to be sold as a medicinal product,
- c. the Product has not already been the subject of a SPC and
- d. the said authorisation is the first authorisation to sell the Product as a medicinal product.

The claimant argued that condition (d) was not met.

The claimant (Generics (UK) Ltd) sought to knock out the SPC on the grounds that:

- i. the patent was invalid over ofloxacin, and further or alternatively
- ii. the SPC was wrongly granted because it was not based as it should have been on the first marketing authorisation, namely the earlier marketing authorisation for the racemate, ofloxacin (which contains levofloxacin)

Jacob LJ gave the lead judgment, with which Ward & Lloyd LJJ concurred.
Outcome

Obviousness

Jacob LJ cautioned himself that there is only one test, namely that in Art 56 EPC and s3 Patents Act 1977, "Was the invention obvious to a person skilled in the art having regard to any matter which forms part of the state of the art?" and that while a judge made test of formula," can be helpful, "they are only tools for answering the statutory question. Adherence to any rigid formula can be a mistake." He then proceeded to adopt the Windsurfing test, as restated by him in Pozzoli. He said that the Windsurfing/Pozzoli test merely makes explicit that which is implicit in the statutory test and it is consistent with the European Patent Office's problem/solution approach.

Generics' case was that resolution of ofloxacin was "obvious to try". The prior art was a poster displayed for some two hours (while disputed at first instance that the poster had been made available to the public, this was not appealed), which showed how the enantiomers of flumequine were made. Generics' case required the skilled person to recognise that the same method would probably work for ofloxacin, to follow this up by experiment and find that it did work. The judge found that flumequine and ofloxacin were structurally different, and the method and agents shown for resolving flumequine were unusual, so knowing how flumequine could be resolved would not make resolving ofloxacin obvious to try.

The judge accepted that the skilled person could have found out the method of obtaining levofloxacin without undue effort but he was not satisfied that he would have known that method as part of his common general knowledge. The skilled person has certain information in his head but other information is not carried in his head, merely being readily at hand: where he knows that he can find it if he needs to. Jacob LJ said that the latter should not be regarded as part of the common general knowledge unless there is a particular reason for the skilled person to refer to it.

Kitchin J had not erred in principle. Jacob LJ added: "Only a curmudgeon would say there was no invention here." The patent was valid.

SPC validity

It may take close to the life of a patent for a medicinal product to achieve marketing authority such that the product can be sold and the pharmaceutical company can start to make a return on its investment. SPCs may be granted, extending the period of exclusivity available under the patent, thereby giving makers of medicinal products an incentive. An SPC may extend the period of exclusivity by five years from the expiry of the patent, but up to a maximum of 15 years from the time when the "Product" first receives marketing authorisation.

The "Product" is defined by the SPC regulation as "the active ingredient or combination of active ingredients of a medicinal product."

Where a racemate has therapeutic effect, it may be the case that one of the enantiomers has a greater therapeutic effect than the other; in some cases one enantiomer has no effect at all; and in other cases one enantiomer might have a toxic or other effect (as the (-) enantiomer of citalopram had in Generics v Lundbeck). Here, the R(+) enantiomer of ofloxacin had some activity, but levofloxacin was markedly more effective (and was less toxic, so could be given in larger doses).
Generics' case was that the active ingredient in the ofloxacin racemate was the levofloxacin enantiomer. It followed that the marketing authorisation for ofloxacin was based on levofloxacin as the active ingredient. On this basis, the first marketing authorisation of levofloxacin was actually the marketing authorisation for ofloxacin (given in 1985 in Germany and in 1990 in the UK), whereas Daiichi relied on the marketing authorisation for levofloxacin itself (given in 1997 in the UK).

Jacob LJ's view was that that argument was unfounded since the "product" is the "active ingredient or combination of active ingredients" as the case may be. In the case of ofloxacin, this was the combination of the two enantiomers, since both had some effect (albeit that levofloxacin had a far greater effect). Had the other enantiomer been biologically inactive, it might have been the case that the 1985/1990 authorisations ought to be considered to be for the same active product, but here, both enantiomers had some effect.

It was submitted that ofloxacin should be treated as no more than levofloxacin with an impurity. However, Jacob LJ saw this is wholly unrealistic: the racemate and the enantiomer are treated as different by patent law (hence the enantiomer is not anticipated by the racemate) and by the law controlling the marketing of medicines. Jacob LJ considered this conclusion to be "acte clair" and so did not require a reference to the European Court of Justice.

The validity of the SPC was upheld.

**Comment**

It is now firmly entrenched in UK patent law that an enantiomer is not anticipated by its previously available racemate (so long as what is claimed is the enantiomer in isolation – see, for example, *Generics v Lundbeck* first instance decision).

The implication of this judgment is that if a product is capable of separate patent protection then it is also to be regarded as a new product for the purposes of the SPC Regulation. Accordingly, a patentable enantiomer which is the subject of a new marketing authorisation is entitled to an SPC based on the new authorisation.

It is, perhaps, still a live question as to whether an enantiomer which is the subject of a new patent and a new marketing authorisation can have a new SPC even where the enantiomer which is not the subject of the patent is completely inactive (which was not the position in this case), or whether in those circumstances the inactive enantiomer is to be regarded as a mere impurity.

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